Diagnostic and Interventional Imaging (2015) **96**, 807—821

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Hemostastic embolization in oncology

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KEYWORDS
Hemostatic embolization;
Tumor rupture;
Hemorrhage

Abstract Several mechanisms predispose to bleeding in neoplastic disease. This is all the more serious as it often occurs on a background of medically vulnerable patients and the magnitude of the bleed may lead to hemorrhagic shock or acute respiratory distress as a result of hemoptysis. It often carries a poor prognosis, even if the acute episode has been controlled, as bleeding due to rupture of a tumor often indicates an advanced stage of the disease, and also because tumor rupture carries a risk of metastatic spread including peritoneal carcinomatosis. The risk of recurrent bleeding is also not insignificant. In most cases, endovascular hemostatic embolization is the first line palliative treatment.

Malignancy is the leading cause of death in France and is responsible for approximately 30% of deaths [1]. In an oncology context, progression to multi-organ failure may occur spontaneously either through disease progression, by extension of the malignancy or more acutely through infection or a bleeding or thromboembolic complication. We offer a review of the interventional radiology embolization methods used for bleeding complications in an oncology situation.

Pathologic conditions predisposing to bleeding

There are many and often concomitant conditions leading to bleeding in patients with malignancy.

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http://dx.doi.org/10.1016/j.diii.2015.06.008
2211-5684/

Firstly, malignancies themselves are a risk factor for coagulopathy: neovascularization due to growth factors, metastatic bone marrow invasion, thrombotic microangiopathy, disseminated intravascular coagulation or macrophage activation syndrome.

Secondly, iatrogenic causes are often involved. Chemotherapies causing aplasia, prevention of thromboembolic disease, postoperative pseudoaneurysms and a fragile vascular bed following radiotherapy may all be involved.

Thirdly, a tumor may have direct vascular consequences. If it is hypervascularized, tumor rupture may lead to catastrophic bleeding. This applies for example to hemoperitoneum secondary to rupture of hepatocellular carcinomas. The tumor can erode a vessel, combined in variable degrees with mechanical invasion and a local inflammatory reaction. In addition the tumor mass may obstruct venous circulation causing an increase in proximal hydrostatic pressure, resulting in varices and shunts which may rupture.

Hemoptysis

General details

The severity of hemoptysis is due to several factors: underlying patient circumstances, extent, consequences on coagulation and far more rarely, hemorrhagic shock. Malignant tumors are responsible for approximately 30% of hemoptyses [2], and 30% of patients suffering from lung cancer will develop hemoptysis, 10% of which will be massive [3].

The bronchial arteries are responsible for over 90% of hemoptyses requiring endovascular or surgical intervention [4].

The systemic vascularization of the lung parenchyma is extremely variable and consists of bronchial and also non-bronchial arteries. The so-called modal bronchial arterial organization consisting of a right bronchial artery arising from a right broncho-intercostal trunk and two left bronchial arteries arising from the T5-T6 descending thoracic aorta only account for 25% of cases [5]. In addition to the variability in number and topography of these systemic bronchial arteries, interventional radiology also needs to take account of the features described below.

Other systemic non-bronchial arteries may contribute to lung vascularization. Physiologically, the only other systemic arteries liable to be involved are the arteries from the area of the triangular ligament. On the other hand, when a previous history of pleural disease is present, symphysis may result in recruitment of chest wall arteries. These have the specific feature of not reaching the lung parenchyma through the hilum but through the pleura. The presence of pleural thickening (over 3 mm) near the vascular entry point is an indirect sign facilitating their detection [6]. The inferior phrenic, internal thoracic arteries and thyrocervical trunk are, for example, occasionally involved.

A rich anastomotic network exists both between these bronchial arteries and also with almost all of the systemic mediastinal arteries. In lung disease causing hemoptysis, branches arising from this network can be involved and hypertrophy. This is a risk factor for recurrent hemoptysis and these anastomoses must be treated during embolization (for example an interbronchial anastomosis).

This network can also give rise to ischemic complications. The most worrying is spinal ischemia due to accidental embolization of branches of the intercostal arteries which contribute to the formation of the anterior radicular artery, the largest of which is the artery of Adamkiewicz, which also has very variable topography [7—9]. This arises between levels T9 and T12 in 75% of cases, usually on the left (65 to 80%), although not uncommonly it may originate as high as level T5. Identifying this artery during angiography is therefore recommended before an embolization procedure is started. Even where it is looked for however, it is not always straightforward to detect because of its small diameter and the intercostal vascular steal effect caused by the bleed [10]. Radiologists should therefore be extremely vigilant and examine angiographic images carefully for any washout flow, which represents reversal of the circulation in these arteries that supply the spinal cord [5].

Myocardial, esophageal, bronchial and tracheal ischemia may also occur through the same mechanism.

CT angiography

Chest CT angiography plays a major role in the investigation of hemoptyses. The purposes of this investigation are to assess the consequences of intra-alveolar hemorrhage, to diagnose underlying disease and to construct a pretreatment chest arterial map [11]. CT angiography therefore needs to be carried out with sufficiently concentrated iodine contrast medium (350 mg/dl), delivered at a sufficient flow rate (at least 4 ml/s) [11]. In order to analyze both the pulmonary and systemic vascularization, the image should be recorded in the early systemic arterial phase, if possible using a bolus arrival detector. In addition, because of the small diameter and considerable variability in topography of the arteries examined, thin sections covering a volume ranging from the base of the neck to the renal arteries are essential.

Intra-alveolar hemorrhage appears on CT as a combination of ground glass lesions with blurred margins and filling of the respiratory tract with liquid opacifications [11]. These hemorrhages may mask an underlying lesion, particularly a small cancer and the state of the parenchyma should therefore be checked distant to the episode of bleeding.

The features of pathological systemic blood vessels supplying the lung and therefore, potentially responsible for hemoptysis are a combination of increased diameter (over 2 mm) [12], excessive tortuosity, a systemic-pulmonary shunt and very occasionally, extravasation of contrast medium [13]. The lung parenchyma may also enhance both on CT and on arteriography [14]. From a prognostic perspective however, dilation of the bronchial arteries correlates poorly with their risk of bleeding [15].

Physiologically, capillary anastomoses exist between the bronchial and pulmonary arteries and account for 5% of cardiac output [16]. During increased demands on the systemic vascular system these communications between a low-pressure pulmonary network and a high-pressure systemic network hypertrophy. The pressure difference then makes the anastomoses fragile and occasionally result in aneurysm formation.

In the majority of cases, the target vessel is a bronchial artery (Fig. 1) and less commonly a pulmonary artery (Fig. 2) if part or all of the bleeding is suspected to arise from the pulmonary circulatory system. CT therefore guides embolization.

Embolization

Because of target vessel size, microcatheters often need to be used.

Embolization should be sufficiently selective to avoid restoring supply from arterial anastomoses which would promote recurrence of bleeding and which is occasionally more difficult to access by an endovascular approach [5]. The embolization site, however, must not be too peripheral in order to reduce the risk of ischemic complications. Conversely, access to the proximal part of the embolized arterial trunk should be maintained in view of the possibility of a recurrent bleed.

The embolization agents used are mostly non-resorbable microparticles (of diameter over 200 μm) and Onyx® [4,17,18]. The use of metal coils alone should be avoided in this situation, firstly because they carry a risk of allowing anastomotic flow to return from distally and therefore a risk of recurrent bleed, and secondly because they represent an obstruction if endovascular treatment needs to be repeated. They may be used as a supplement if flow is not entirely abolished by other techniques. It should be noted that the recurrence rate was 50% in the study published by Witt et al., which used coils as the only embolization agent compared to only 20% reported in the study by Garcia-Olivé et al. in which the radiologist had a free choice of materials [19,20].

Hayakawa et al. [21] initially suggested that this technique was less useful in the context of malignancy than for benign causes of hemoptysis, although several studies [3,19,20,22] have subsequently shown that endovascular embolization is an effective palliative treatment for hemoptysis in oncology. The two most recent studies reported clinical success rates of close to 90%, although the prognosis of these patients remained poor, with a 64% mortality rate at one year [19,20].

Rupture of hepatocellular carcinoma

General details

Hepatocellular carcinoma (HCC) is the third leading cause of cancer deaths in the world [23,24]. Its worldwide incidence is increasing because of the spread of hepatitis B and C virus infections [25,26]. This common cancer is a public health problem, particularly in Eastern Asia and sub-Saharan Africa, where the incidence rates were 36.9 and 79.4/100,000 men in 2002 compared to only 1.8/100,000 men in Holland [27].

Whilst HCC can be indirectly responsible for bleeding complications as a result of decompensation of underlying cirrhosis, it may be a direct cause due to tumor rupture. This is a relatively rare complication with reported incidences of 3.5% on the UK and 12.4% in Thailand [28,29]. It is however serious and median survival is less than 1 month if the cause is not treated [30].

The clinical presentation is typically a combination of sudden-onset epigastric or right hypochondrial pain, hemorrhagic shock and abdominal distention. Occasionally the tumor may rupture into the biliary tract and cause a sudden-onset picture of epigastric or right hypochondrial pain associated with cholestasis jaundice, melena and hematemesis [31].

Figure 1. Severe hemoptysis not controlled by medical and endoscopic treatments in a patient with lung cancer: a: enhanced chest CT. Hilar mass developing next to the right upper lobe bronchus; b: arteriography of the right intercosto-bronchial trunk showing hypervascularization in the territory of the tumor (arrow); c: arteriography after embolization with non-resorbable 250 μm diameter particles. The intercostal artery is preserved.

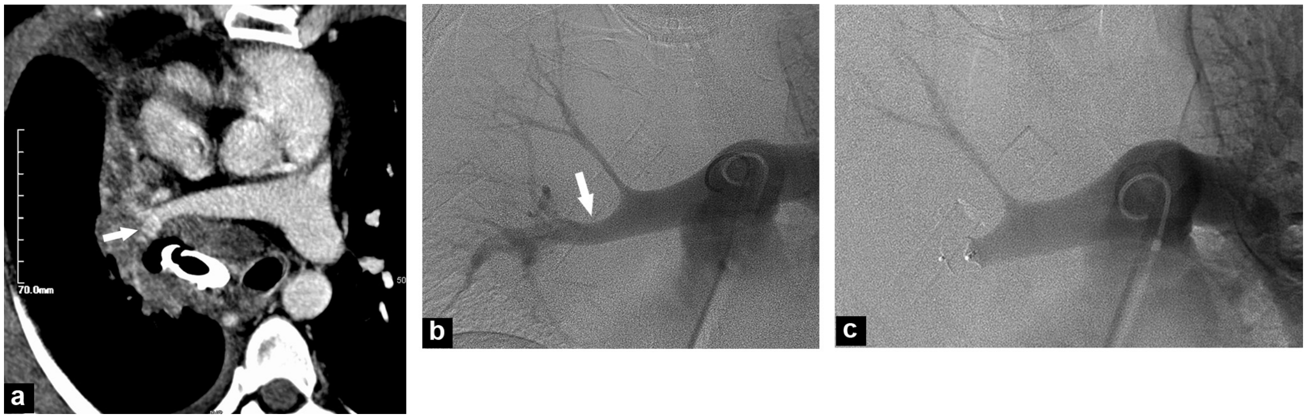

Figure 2. Severe hemoptysis not controlled by medical and endoscopic treatments in a patient with hepatocellular carcinoma with lung and mediastinal metastases: a: enhanced chest CT: cavitating hilar mass in contact with a interlobar artery near its border (arrow); b: pulmonary arteriography: laminar appearance of the interlobar artery (arrow); c: result after obstruction of the interlobar artery with an Amplatzer 12-mm diameter Plug.

The most widely accepted mechanism for this complication is invasion of the hepatic veins by tumor, impeding venous drainage of the HCC and resulting in a large rise in intra-tumor pressure and hemorrhage, initially within the tumor, which breaks through the HCC [32].

The risk factors for rupture are hypertension, underlying cirrhosis, large tumors (over 5 cm), tumor protrusion on the surface of the liver, vascular thrombosis and extra-hepatic tumor extension [30—33].

In this situation, excision surgery can only rarely be considered because of the many concomitant contraindications of portal hypertension, hepatic encephalopathy, ascites, hepatic reserve function and small estimated volume of postoperative residual liver. Only 6 out of 54 patients (11.1%) were eligible for surgery in the study reported by Jin et al. [34].

The alternatives to surgery are hepatic artery ligation, suturing or packing.

Embolization

Embolization is likely to be as effective and less damaging in these medically vulnerable patients, as it is less aggressive and allows more selective treatment.

The technique involves obtaining peripheral arterial access and then catheterizing the feeder artery to the bleeding tumor as selectively as possible. The embolization agents used include resorbable gelatin particles. Convention chemoembolization can also be carried out if the patient is not hemodynamically unstable and if the drug is readily available (Fig. 3).

Whilst embolization can be used in a larger population of patients than surgery, it also has its contraindications and the technique could only be used in 52% of patients rejected for excision surgery in the study reported by Jin et al. [34]. It is essential to assess hepatic reserve as the most serious consequence of arterial embolization is hepatocellular failure. Laboratory liver function tests and Child-Pugh or MELD scores are essential in the pre-treatment assessment. Obstructive portal thrombosis is a contraindication to arterial embolization. If the biliary tract is dilated in the target segment, the risk of ischemia and cholangitis has to be balanced against the severity of the bleed. Unlike non-bleeding lesions, there is no consensus on the management of these patients and it would appear difficult to apply the Barcelona Clinic Liver Cancer guidelines [35] strictly to these patients as this is an immediately life-threatening complication in the very short term.

The post-embolization syndrome, which is a combination of pain, small spikes of fever, nausea and vomiting lasting a few hours to a few days occurs in almost all patients.

Embolization is effective and controls bleeding in 94% of cases, achieving a significant extension of survival [33]. In the study reported by Jin et al. the 2-, 4- and 6-month survival rates were better in the embolization group (36%, 20% and 20% respectively) than in the ''supportive care'' group (8.7% and 0%) [34]. Median survival of patients in the study reported by Kirikoshi et al. was 224.8 days compared to only 13.1 days in the ''conservative treatment'' group [33]. The main cause of death in the control group in this study was a recurrent bleed (72%), whereas the main cause of death in the embolization group was hepatocellular failure (67%).

Poor prognostic indicators after treatment of the episode of bleeding are a raised serum creatinine, the need for vasopressor amines, a raised bilirubin and a large tumor size (over 7 cm in size) [33,34].

The poor prognosis of ruptured HCC even when the bleeding has been controlled is due to several factors: the bleed often indicates locally or distant advanced stage of the tumor and decompensation of the cirrhosis is a common complication of bleeding. Even once the acute episode has passed, the risk of peritoneal spread inherent to tumor rupture is sufficiently high to represent at least a temporary contraindication to liver transplantation [36].

Other primary hemorrhagic liver tumors

Whereas HCC is by far the most common cause of tumor bleeds in liver disease, the tumor most commonly responsible for bleeding outside of the context of cirrhosis is benign, since it is an adenoma [37].

Cholangiocarcinoma is the second most common primary malignant liver tumor and contains a large fibrous

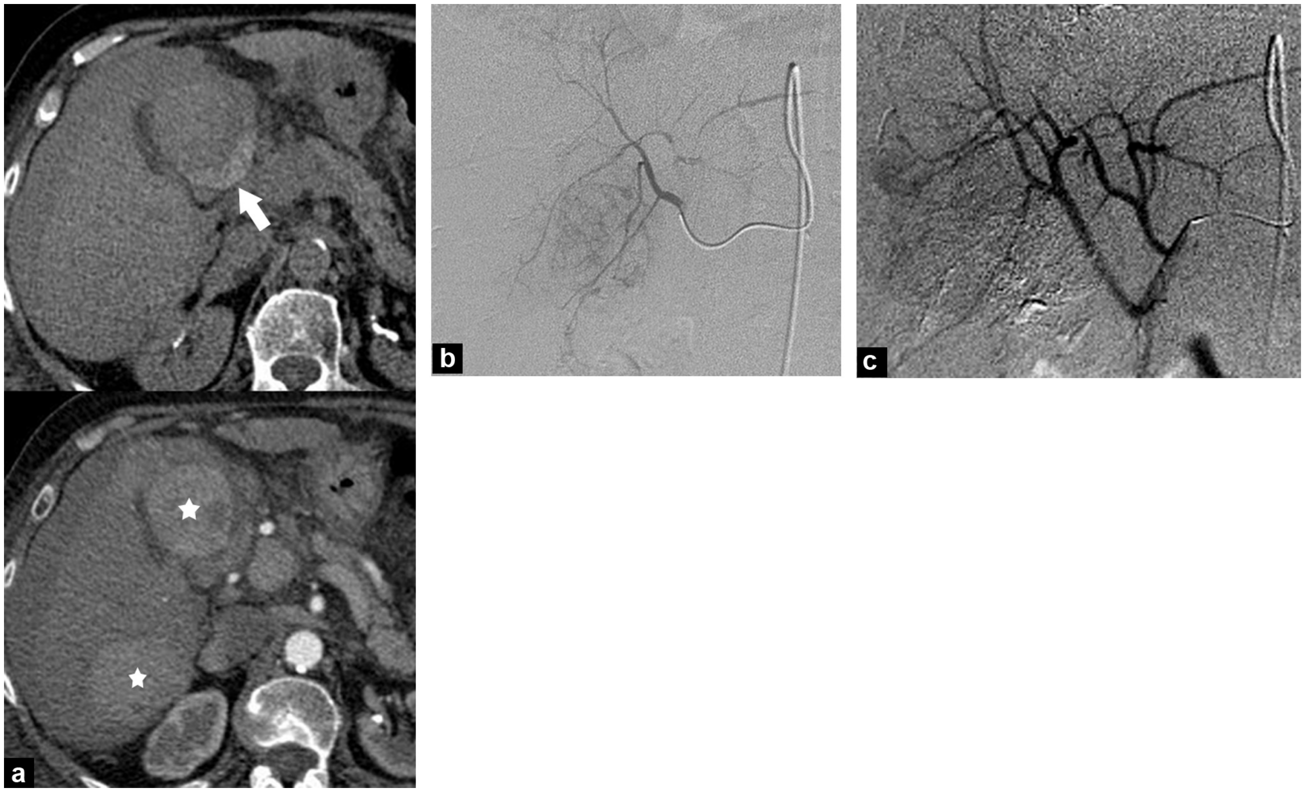

Figure 3. Sudden-onset severe abdominal pain in a patient with clinical signs of cirrhosis: a: abdominal CT with and without enhancement in the arterial phase. Dysmorphic liver with 2 hyperarterialized tumors (stars) and a hemoperitoneum. The sentinel hematoma (arrow) in contact with the lesion in segment IV indicates the hepatocellular carcinoma responsible for the bleed; b: pre-embolization arteriography. Selective catheterization of the branch supplying segment IV confirms the presence of tumor enhancement; c: post-embolization arteriography. In the absence of hemorrhagic shock, Lipiodol tumor embolization could be administered in this emergency situation.

component, explaining why bleeding is a very rare complication with this type of tumor.

The potentially hemorrhagic primary malignant liver tumors also include primary hepatic angiosarcoma (PHA). This only represents 2% of primary malignant liver tumors but it is the most common malignant mesenchymal tumor, in front of epithelioid hemangioendothelioma, one of its differential diagnoses, and other sarcomas [38,39]. This is a richly vascularized tumor, which develops from sinusoid capillary endothelial cells. Most cases are idiopathic, although some carcinogens including vinyl chloride, thorium dioxide and arsenic are occasionally implicated, together with prolonged exposure to anabolic steroids. The male-female sex ratio is 3:1. This disease carries a poor prognosis and median survival at the time of diagnosis is 5 months [40]. There are several obstacles to its diagnosis: the non-specific clinical presentation, lack of specific biological marker, variable appearances on imaging (multiple nodules, a single or predominant mass or diffuse infiltration of the liver parenchyma) [40,41]. In addition, ultrasound or CT-guided percutaneous biopsies are occasionally negative, incorrectly suggesting an alternative histology and may even be dangerous due to potential bleeding complications. If PHA is suspected it is preferable to take laparoscopic surgical biopsies. Synchronized metastases are common and are typically found in the spleen and lungs.

Because of the rich vascularization of this tumor, it is not unusual to encounter spontaneous hemorrhagic complications and in 26.6% of cases the presenting sign is a hemoperitoneum, which may also recur [42,43]. Simple embolization (Fig. 4) or chemoembolization are the first-line etiological treatments for a bleeding PHA [44]. The gold standard treatment in the absence of bleeding combinations or after bleeding has been controlled is poorly defined and involves excision surgery, although this is rarely possible as synchronous extra-hepatic metastases are often present.

Rupture of intra- and extrahepatic metastases

Secondary liver tumors are rarely responsible for bleeding compared to primary liver tumors. Whilst bleeding metastases from many primary tumors have been described, lung and renal carcinomas and melanomas are the tumors that most often cause bleeding [45]. This situation is far rarer although it is managed differently to the HCC as no underlying liver disease is present. In the case of a hemoperitoneum however, these patients also have a poor prognosis and almost none survive over 6 months [46].

Given the rarity of bleeding liver metastases, a relatively non-specific clinical presentation with variable proportions of shock, sudden-onset severe abdominal pain and a surgical abdomen points towards differential diagnoses such as a perforated peptic ulcer [47]. Imaging can occasionally refine

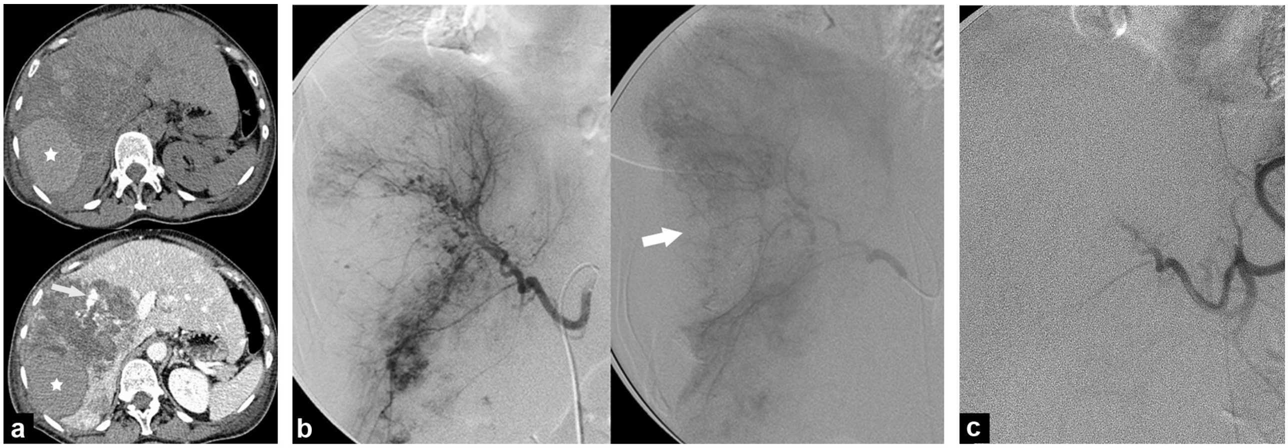

Figure 4. Spontaneous bleeding of a hepatic angiosarcoma: a: abdominal CT before and after contrast enhancement. Heterogeneous hypovascularized mass with blood lakes (arrow) combined with an intrahepatic hematoma (star); b: in the arterial phase (left image), arteriography shows predominantly peripheral enhancement appearing as blood lakes. In the venous phase (right image) the avascular zone (arrow) persists and shows the intra-hepatic hematoma; c: post-treatment appearances after embolization with resorbable particles.

the diagnosis by showing a bleeding liver lesion, spontaneous sub-capsular hematoma, hemoperitoneum or primary tumor.

In common with the HCC, the diagnosis can occasionally be supported by active extravasation contrast medium, and in some cases a heterogeneous collection contiguous with the lesion with a density of 50—60 Hounsfield units indicates a sentinel clot and therefore a recent bleed [45—49].

Extrahepatic metastases can also rupture and cause intraperitoneal or retro-peritoneal hemorrhage or bleeding into the gastrointestinal or urinary tract. The histological tumor types responsible are the same as for intrahepatic disease. These are relatively non-specific and the first-line treatment of uncontrolled bleeding is also endovascular embolization (Fig. 5).

The diagnosis is considerably easier when prior imaging shows a pre-existing metastasis.

Rupture of a retroperitoneal tumor

This is a rare pathological condition. Zhang et al. reported 101 cases of spontaneous perirenal hemorrhage in a meta-analysis based on English-language publications between 1985 and 1999 [50]. In decreasing orders of frequency the causes of spontaneous perirenal hematoma are angiomyolipomas, renal cell carcinomas and polyarteritis nodosa [50—52]. Clinical symptoms are non-specific and include Lenk's triad, which is a combination of sudden-onset unilateral lumbar pain, lumbar swelling and hemodynamic abnormalities and is present in 50% of cases. Hematuria is often absent [52,53]. The pathophysiological mechanism involving rupture of a renal tumor is poorly understood. Angimyolipomas and renal cell carcinomas have the specific feature of being richly vascularized, which appears to be a risk factor for bleeding. Papillary carcinoma, the second most common subtype of renal cell carcinoma in order of frequency after clear cell carcinoma very rarely bleeds, as it is hypovascularized [54,55].

Some authors have attributed the cause of a bleed to direct erosion of the renal vessels or renal capsule by the tumor, whereas others have suggested that in the same way as for HCC, venous invasion causes a rise in pressure within the tumor, predisposing to rupture. In addition, tumor rupture occurring during hemodialysis may be attributable to the anticoagulation required because of the extracorporeal circulation [56].

The investigation of choice in this urgent situation is computed tomography [57]. Identifying a tumor underlying a perirenal hematoma may be difficult, as the volume of the hematoma often masks small tumors. This process is made even more difficult when concomitant acquired polycystic disease is present in the dialyzed kidney. This has a prevalence of 33% in patients with end-stage renal failure, particularly as these patients are at risk of malignancy, as the prevalence of renal cell cancers in this group is 4.2% [58].

Irrespective of the underlying disease, renal embolization is the first line emergency treatment if the bleeding is poorly tolerated clinically (Fig. 6). This often succeeds in obtaining hemostatic embolization and can identify the lesion responsible. If it fails, the ultimate recourse is hemostatic nephrectomy.

Subsequent treatment is guided by the cause. It is important to highlight that if no cause is found on radiological investigations it is highly likely that a malignant tumor is present. Caution, regular monitoring and even nephrectomy are required [59,60].

Spontaneous ruptures of pheochromocytomas are also extremely rare but have a mortality rate of 32% [61]. This is explained not only by the risk of bleeding but also and particularly at the risk of potentially fatal catecholamine release as a result of surgery. Excision surgery requires careful patient preparation with non-selective adrenergic receptor antagonists in order to stabilize blood pressure and reduce the risk of cardiac arrhythmia [62,63]. If it is not possible to prepare the patient before excision surgery for a ruptured pheochromocytoma, the mortality rate reaches

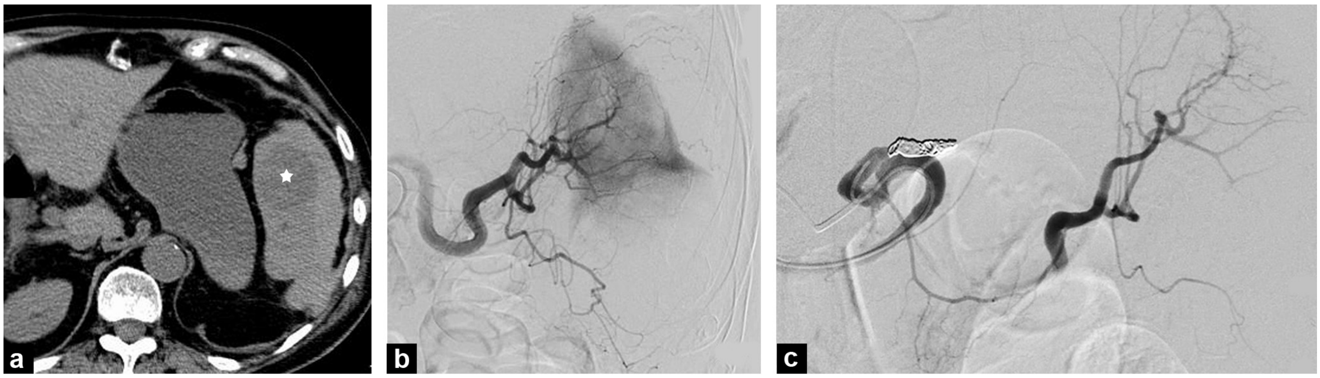

Figure 5. Rupture of spleen metastases of a melanoma: a: abdominal CT without enhancement. Subcapsular splenic hematoma in contact with a spontaneously hypointense intraparenchymal mass (star); b: splenic arteriography. Hypovascular mass in the inferior pole of the spleen appearing as a spur sign; c: splenic arteriography. Post-treatment appearance after proximal obstruction of the splenic artery with coils analogous to the preventative embolization technique for traumatic injury to the spleen at high risk of rupture. Proximal embolization reduces the intrasplenic pressure and avoids infarction because of collateral supply from the gastro-epoploic and pancreatic arcades.

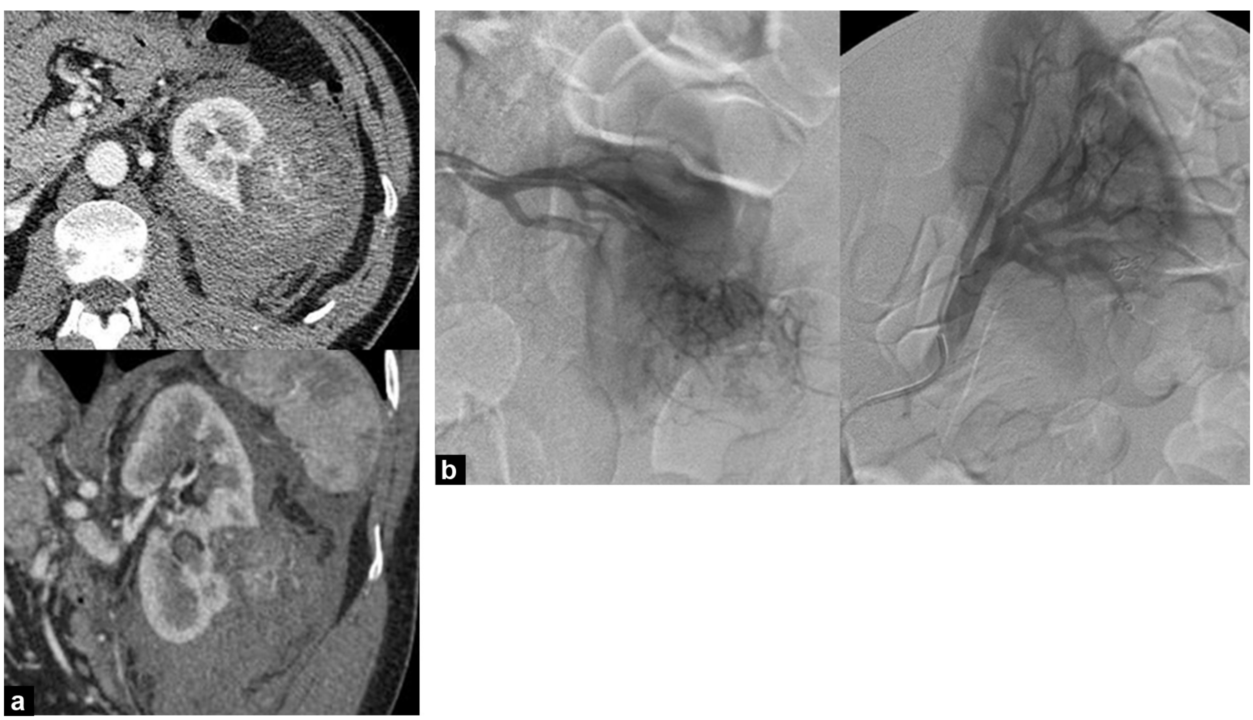

Figure 6. Renal cell cancer presenting with hemorrhagic shock: a: CT after contrast enhancement, axial and coronal view. Clearly delineated mass on the external border of the left kidney, which is hypovascularized and surrounded by a large hemoperitoneum; b: hemostatic embolization. Pre-procedure angiography (left image) shows rich tumor neovascularization. Interruption of flow in the tumor branch after embolization on the right (non-resorbable particles and coils).

44.7% [64]. Embolization is also the treatment of choice for a bleeding pheochromocytoma as it allows planned excision surgery to be carried out.

Hematuria and bladder cancer

Macroscopic hematuria, which is classically painless and occurs at the end of voiding, is the presenting symptom of bladder cancer in almost 80% of cases [65] and can also occur during the natural history of the disease after its initial stages. The causes of hematuria in this situation are multiple and often interlinked: primary tumor bleed, radiation or chemical cystitis, severe infection or the co-existence of other pelvic cancers [66]. The bleed is also maintained by the anti-coagulant effect of urokinase. The consequences of hematuria may be a globus vesicalis, obstructive renal failure or even hemorrhagic shock.

Many treatments can be used for these cases of hematuria, including oral administration of ε–aminocaproic acid, intravesical irrigation with alum, instillations of prostaglandins, fractionated radiotherapy, bladder diversion and palliative excision. Despite this wide range of methods used, controlled studies providing a solid basis for the approaches to treatment are lacking. Interventional radiology offers two techniques: embolization and intra-arterial chemotherapy with mitoxantrone. These have the common feature of not requiring general anesthesia. They also involve a similar vascular approach, puncturing the common femoral artery followed by cross-catheterization using the Seldinger Technique, with the aim of selectively catheterizing the anterior dividing trunk of the internal iliac artery in order to spare the superior gluteal branches [67,68]. The embolization agents used in preference should allow the procedure to be repeated if the bleeding recurs. Wherever possible, therefore, metal coils should be avoided. The most common complications are pain in the gluteal region and temporary urinary disturbances. Lasynecrosis is the most worrying complication, although this has only been reported in cases of severe pelvic trauma [66—69].

Intra-arterial chemotherapy involves an intra-arterial infusion of mitoxantrone at a dose of 20 mg/m^2 body surface area, over a period of 1 to 2 hours, which may be repeated [70].

Textor et al. compared the two techniques in a non-randomized study [69]. Although the bleeding control (80 and 93.3%) and recurrence rates (21.4 and 30.8%) were similar in both groups, severe complications only occurred in the ''embolization'' arm and post-treatment pain was also more common in this group (90.9% versus 19.4% in the ''chemotherapy'' arm). On the other hand, the time required to achieve control of the bleeding was less than 24 hours in the ''embolization'' group compared to 4 to 15 days in the ''chemotherapy'' group [69]. It appears therefore that embolization is an appropriate technique for acute, life-threatening hematuria, whereas chronic hematuria can be treated by intra-arterial chemotherapy. No studies have described the combination of this technique with intra-arterial chemoembolization.

Arterio-ureteric fistula

The incidence of this disease is increasing and is probably underestimated. Risk factors for an arterio-ureteric fistula are a previous history of abdominal or pelvic oncologic or vascular surgery, urinary shunt surgery, prolonged use of a bladder catheter, a previous history of radiotherapy or a vascular stent [71]. By far the most common site of these fistulae is the crossover point between the iliac artery and the ureter. In this area the proximity of these structures make their walls vulnerable to inflammatory and fibrotic reactions and where relevant, radiation vasculitis, all of which are responsible for fistula formation [72]. Although this is a rare condition it is important not to miss its possible diagnosis, as the disease-specific mortality without treatment is 58% and a delay in diagnosis is a major poor prognostic indicator [71—73].

The predominant symptom is hematuria, which occurs in all patients and may be either microscopic or macroscopic. Although it is often not particularly heavy but is recurrent, it may involve catastrophic bleeding. Hematuria is the only symptom in 74% of cases and is combined with lumbar pain or signs of infection in 17% and 7% of cases respectively [71].

The diagnosis can occasionally be made by the usual investigations carried out for hematuria, although only a small percentage of conventional investigations are contributory (42% for CT, 14% for ultrasound and 4% of cystoscopy) [71].

The reference diagnostic investigation preferred over direct urinary tract opacification methods is iliac arteriography (Fig. 7). It is important to be aware of this specific, rare and often missed condition, as diagnostic errors can lead to a hemostatic nephrectomy being performed, whereas endovascular treatment (usually with a coated stent) achieves excellent results [71].

Rare malignant causes

We also describe below three causes of severe bleeding in a context of malignancy.

Cervical cancer

Although metrorragia is a common presenting feature of cervical cancer, it is extremely rare for this to be hemodynamically threatening (Fig. 8).

Segmental portal hypertension

Advanced pancreatic cancer often causes segmental portal hypertension due to invasion of either the splenic or superior mesenteric vein. The gastric or duodenal varices caused carry a rare but existent risk of gastrointestinal hemorrhage (Fig. 9).

Budd-Chiari syndrome

Very occasionally, extensive tumor disease may compromise hepatic venous drainage and cause true post-sinusoidal intrahepatic portal hypertension (Fig. 10).

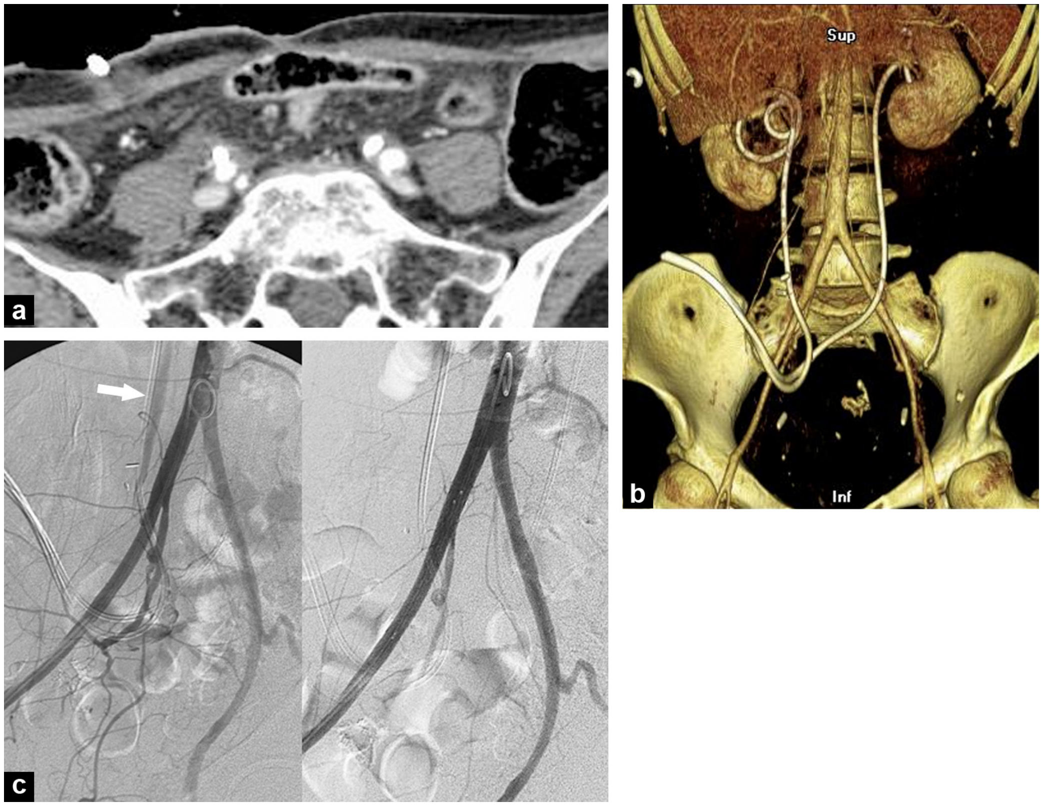

Figure 7. Macroscopic hematuria in a female patient with a previous history of cervical cancer with radiation-induced ureteric damage treated by long-term ureteric bypass: a: CT after enhancement, axial view performed at that time of the bleed not shown extravasation of vascular contrast to the ureters; b: CT after enhancement with volume reconstruction showing the anatomical relationships of the ureteric catheters and two iliac arteries; c: hemostatic embolization. Arteriography shows the fistula between the origin of the right external iliac artery and the ureter (arrow). After deploying a coated stent the arterio-uroteric fistula is abolished.

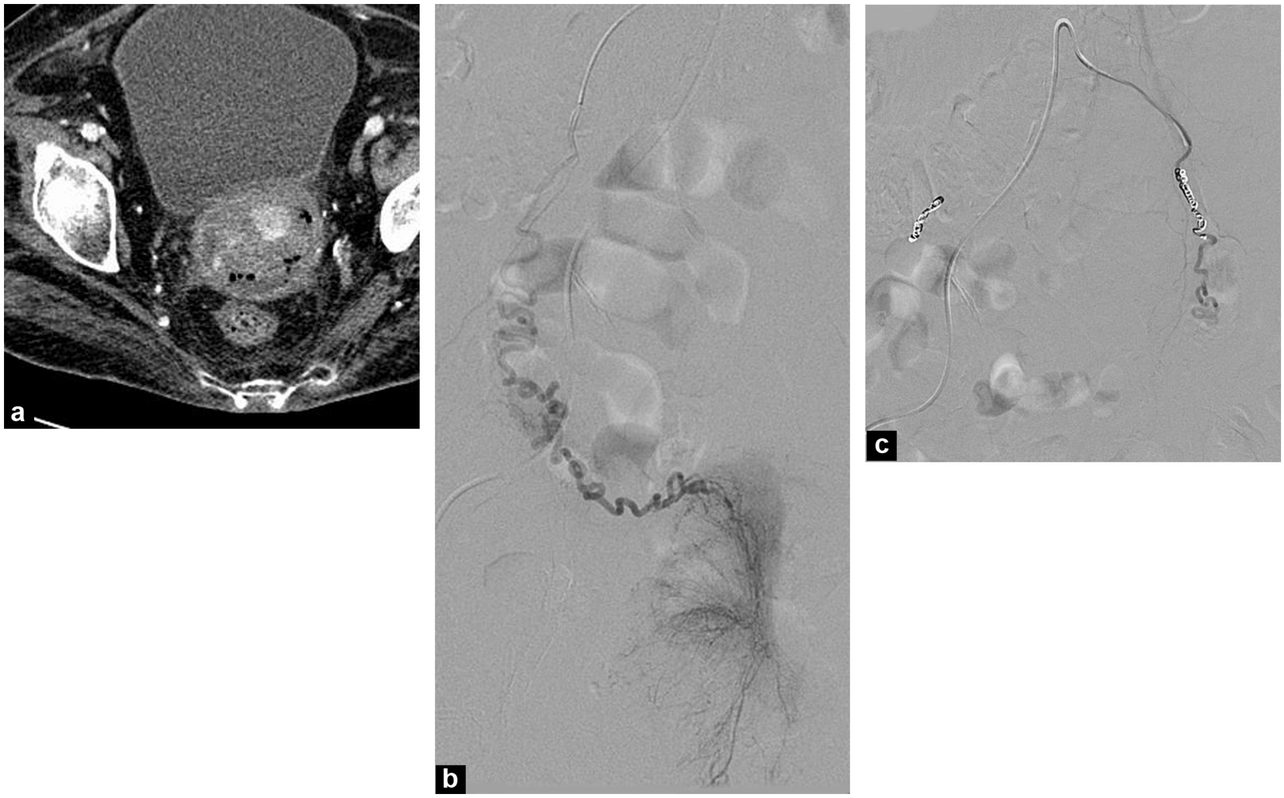

Figure 8. Irretractable metrorrhagia due to cervical cancer: a: CT after enhancement. Hypovascularized infiltrating mass next to the cervix; b: tumor enhancement during selective catheterization of the left uterine artery; c: devascularization of the tumor after embolization (non-resorbable particles and coils).

Figure 9. Recurrent hematemesis in a patient with locally advanced pancreatic adenocarcinoma: endoscopically the bleeding is attributable to duodenal varices: a: enhanced CT axial view (upper image) and frontal MIP reconstruction (lower image). The tumor creates a sheath around the superior mesenteric artery and the mesenteric vein cannot be seen (arrow head), a large intra and peri-pancreatic cavenoma allows reinjection into the portal trunk (white arrow); b: portal recanalizations. Transparietal transhepatic portography (left image) confirms stenosis of the portal trunk (arrow). After passing the obstruction, the opacification of the mesenteric vein correlates well with the CT MIP reconstruction (central image). After deploying a metal stent (right image), the superior mesenteric flow is diverted preferentially to the portal trunk.

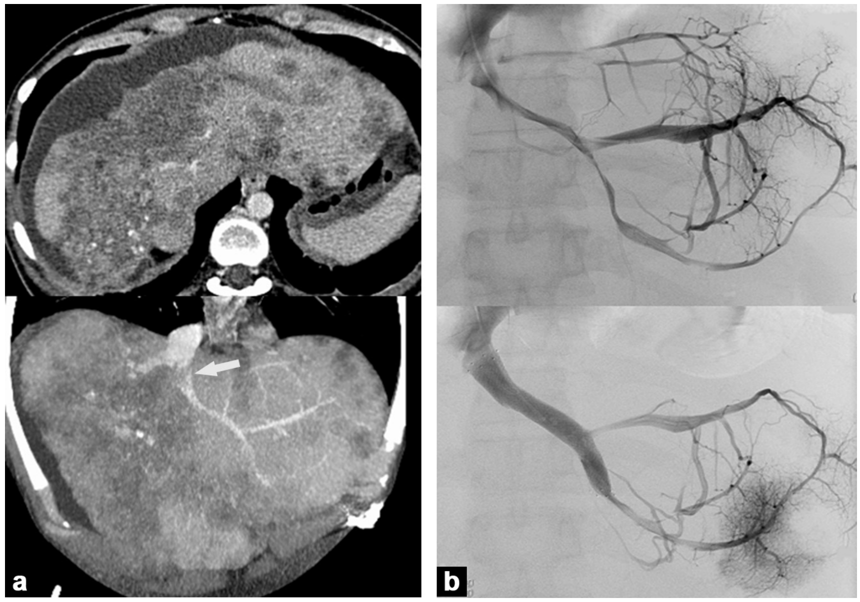

Figure 10. Recurrent hematemesis due to rupture of esophageal varices in the patient with colonic carcinoma and liver extension: a: enhanced CT, axial view (upper image) and frontal MIP reconstruction (lower image). Extensive hepatic tumor infiltration with obstruction of the right and middle hepatic veins and ostial stenosis of the left hepatic vein (arrow); b: left hepatic vein angioplasty through the jugular vein. Deployment of a metal stent releases the proximal stenosis.

Conclusion

Bleeding complications in a context of malignancy have many and often interlinked causes. The immediate risk is the extent of the hemorrhage or its consequences on the functioning of an organ. When the hemorrhage is due to tumor rupture; it also carries a risk of secondary seeding.

In addition to non-specific resuscitation measures, interventional radiology is often the first line hemostatic treatment.

Take-home messages

Context

- Hemorrhages are rare but serious complications of neoplastic lesions.
- The mechanism most commonly involved is tumor rupture.
- Generally, risk correlates with the extent of neovascularization and tumor extension.

Hemoptysis

- Complicates 30% of lung cancers, 10% involve massive hemoptyses.
- The systemic arteries are far more often involved than the pulmonary arteries.
- Embolization should be with particles over 200 μ in size to avoid paradoxical emboli.
- Spinal ischemia is the most worrying complication.

HCC

- Limited surgical options because of the background of underlying cirrhosis.
- Embolization with resorbable particles or chemoembolization.
- The most serious complication is hepatocellular failure and hepatic reserve needs to be assessed before the procedure.
- Relative contraindications: hepatofugal portal flow, biliary tract dilation.

Bladder cancer and hematuria

- No consensus treatment indications
- Embolization is effective for rapid control of bleeding.
- Intra-arterial chemotherapy is suitable for chronic hematuria.

Retroperitoneal tumors

- Embolization is particularly useful for ruptured pheochromocytomas, enabling planned surgery.

Metastases

- The most common primaries: lung, kidney, melanoma.

Arterio-ureteric fistulae

- Risk factors: previous history of abdominal or pelvic oncologic or vascular surgery, urinary tract bypass surgery, prolonged use of a bladder catheter, previous history of radiotherapy or vascular stent.
- Topography: the cross-over between the ileac vessels and the ureters.
- Embolization with coated stent.

Indirect venous mechanism

- Far rarer than tumor ruptures.
- Examples: segmental portal hypertension from pancreatic or bile duct cancers, Budd-Chiari Syndrome due to compression of the hepatic veins.
- Treatment is with angioplasty.

Clinical Case

This 72-year-old woman presents with massive rectal bleeding and macroscopic hematuria, both through the right nephrostomy tube and urethra.

This is a patient hospitalized in urology with a previous history of cervical cancer, treated by pelvic radiotherapy and complicated by right ureteric stenosis, which required surgical re-implantation protected by a nephrostomy. The episode occurred immediately after a failure to change the double J stent.

Questions

1. You carry out an urgent abdominal and pelvic scan without and then with enhancement in the arterial phase (Fig. 11a and b). What is your diagnosis from the images provided to you? Justify your answer.
2. If the CT scan had been negative and showed no other abnormalities, could you have excluded this diagnosis? What would then be the most appropriate investigation?
3. What treatment would you propose?

Answers

1. This is a right common iliac artery fistula, with both the gastro-intestinal and urinary tracts. In the arterial phase, the endoluminal enhancement of the right ureter, last loop of ileum and caecum indicate heavy active bleeding.
2. No, a negative CT does not exclude the diagnosis. Because of the patient's unstable hemodynamic state, iliac arteriography is required.
3. Endovascular embolization of the arterial fistula (Fig. 11c) can be carried out at the stage of the diagnostic arteriography. Deploying a coated stent.

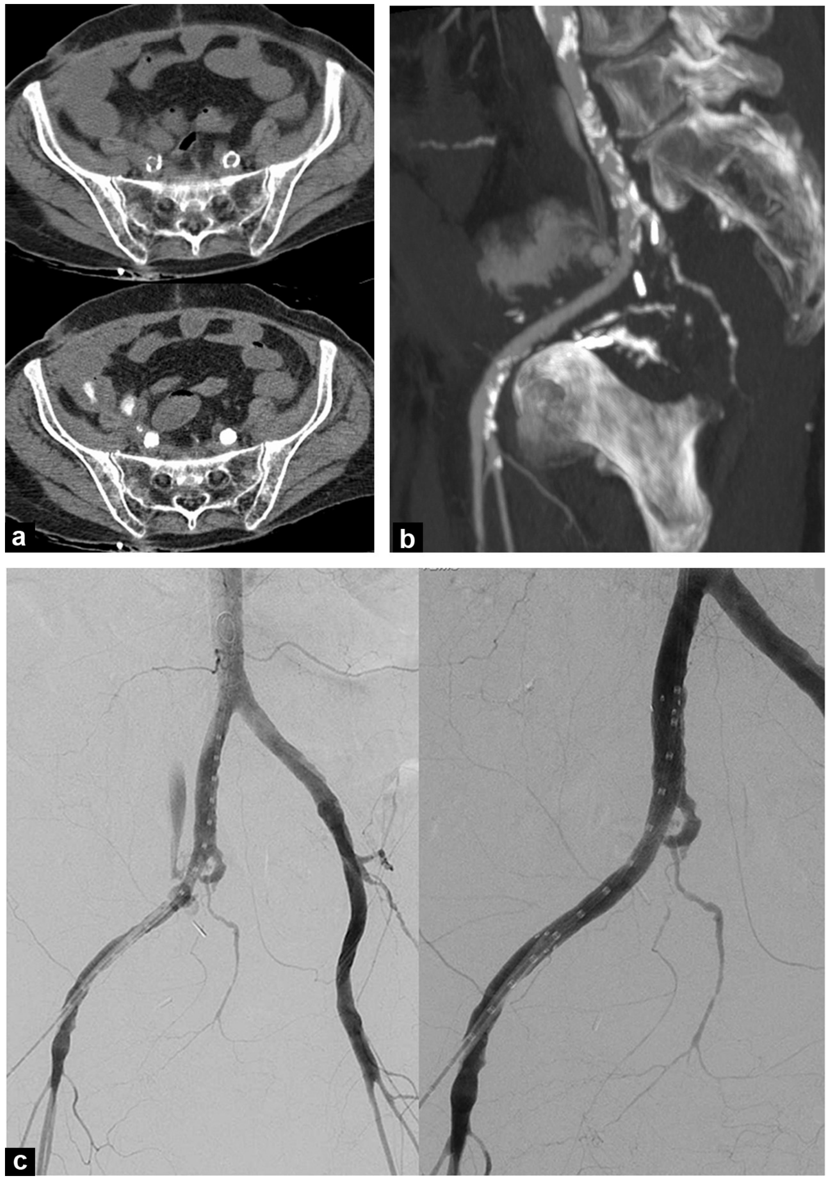

Figure 11. a: abdominal and pelvic CT (upper image) then with contrast enhancement in the arterial phase (lower image); b: abdominal and pelvic CT with contrast enhancement in the arterial phase. Oblique sagittal MIP reconstruction; c: iliac arteriography, pre-treatment (left image) and post-treatment appearances (right image).

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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